Attention-deficit hyperactive disorder with conduct disorder in adolescents and in adults with antisocial personality disorder often coexists with substance abuse disorder. Long-term outcome studies of grown-up children with the disorder show 15% to 40% lifetime rates of drug abuse, which may contribute to and confound assessment of the cognitive disability. It is possible in some cases that comorbidity emerges as an attempt at self-medication.

Several studies indicate a 60% beneficial response to the use of psychostimulants alone. Clonidine and guanfacine, α_2-noradrenergic agonists, have been used to decrease aggression and impulsivity. Nonpharmacologic treatment modalities include psychotherapy, teaching time management, family systems approaches, problem solving, communication training, and learning modification, if a learning disability is present. When a comorbid diagnosis of substance abuse is present, nonpharmacologic treatment may be preferable, including group therapy, individual treatment of substance use disorder and group homes, or residential treatment when indicated.

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Behavioral Genetics

THE APPLICATION OF molecular genetic technology to the study of psychiatric and behavioral disorders has led to a plethora of exciting but often unreplicated findings. Difficulties in the analysis of complex traits and diseases that do not follow simple mendelian patterns are receiving increasing attention but have not deterred the premature acceptance of the validity of reports regarding animals and humans. A mutant mouse model involving a genetic disruption of nitric oxide synthase has been linked to human aggression, and other mouse loci have been related to "anxiety or neuroticism" and to alcohol and morphine dependence. Studies in humans have suggested a link between male homosexuality and a region (q28) on the X chromosome, between attention-deficit hyperactivity and reading disability and a locus on chromosome 6, and between aggression and sociopathy and a point mutation in the structural gene for monoamine oxidase A. Recent studies have indicated that "novelty seeking" in humans may be related to the D_4 dopamine-receptor gene. At least a half dozen loci have been implicated as contributing to schizophrenia, the most recent being a gene on chromosome 6. None of these have received convincing independent replication, however, including the previous "hot" finding linking a band on the long arm of chromosome 5 to schizophrenia.

The story is similar for manic-depressive illness, where recent linkages between the disorder and loci on the short arm of chromosome 18 or the long arm of chromosome 21 are isolated findings marked by increasing skepticism. Whereas there is agreement of a strong genetic contribution to major psychiatric illnesses and to variables of normal human temperament, it has become clear that behavioral phenotypes are exceedingly difficult to determine and that falsely positive determinations of affected status (phenocopies) are extremely harmful to linkage analyses. Until replicated, reports of specific genetic linkage to given psychiatric disorders should be viewed with caution; patients and their families may experience disillusionment when such apparent advances in diagnosis and, potentially, in new therapeutic interventions prove to be illusory.

The genetic heterogeneity of behavioral disorders has underscored the need to supplement traditional familial linkage methods with sib-pair analyses and population-based association studies in appropriate study groups, most ideally those in which a "founder effect" is probable, such as the Finnish, Amish, and French-Canadian populations. When reproducible genetic linkage studies emerge, it is likely that environmental factors will be found to play a major role in the degree to which a given vulnerability gene(s) is expressed. As yet, however, the promise of psychiatric genetics is unfulfilled, and caution is warranted until appropriate methodologic practice is followed.

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